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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20

Application Number: 09/175,713
Filing Date: October 20, 1998
Appellant(s): HERRMANN ET AL.

Lekha Gopalakrishnan
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 18 December 2001.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because, while Appellant states that the pending claims are drawn to modifications of a finite group of chemokines well known in the art, "derived from a chemokine" as defined by Appellant on p. 17 of the specification, means that the chemokine itself can by modified by "any kind of alteration". Claims 6, 7, 8, and 9 encompass molecules identified by hybridization. They also encompass molecules comprising amino-terminal fragments. Thus the group of chemokines encompassed by these claims is not finite and is not limited to molecules known in the art. Claims 17 and 18 contain only the limitation that the chemokine bind the fusin/CXCR4 chemokine receptor and thus are also not limited to a finite group of chemokines known in the art, because variants of the known receptor-binding molecules, as well as, potentially, molecules not yet known in the art are encompassed by these claims.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that Group I, claims 1-5, 10-14, 17, and 18, and Group II, claims 6-9, do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Proudfoot, A., et al. "Externsion of a Recombinant Human RANTES by the Retention of the Initiating Methionine Produces a Potent Antagonist" Journal of Biological Chemistry, vol. 271, no. 5, (Feb. 2, 1996), pp. 2599-2603.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

(a) Claims 1-14, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is set forth in prior Office Actions of Paper No. 8, Paper No. 12, Paper No. 14, and Paper No. 18 and summarized below.

Claims are 1-14, 17, and 18 are drawn to a genus, i.e. polynucleotides encoding amino-terminal modified chemokines. As defined by Appellant on p. 17, these polynucleotides include

not only those known in the art, but also molecules derived by alterations to the known molecules. Claims 6-9 limit only to a subset of species and include variants comprising fragments as well as species identified by hybridization. All of the claims encompass molecules having more than one amino-terminal modification. For claims 1, 5-14, 17, and 18, said modification is selected from a group of different modifications. Thus, the claims encompass molecules that are widely variant in structure and further encompass a potentially infinite number of species. Appellant has disclosed methods of making four species and the functional characteristics of one of these species, met-SDF-1-beta, which exhibits an enhanced function relative to the native molecule. The disclosure of four closely related molecules, each a modified form of SDF-1 alpha or beta, and the functional characteristics of only one, are insufficient to describe the genus, which includes not only specified chemokines but also species comprising additions, insertions, deletions, mutations, substitutions, and replacements, as well as amino-terminal additions of varying lengths and compositions. Appellant has not described any specific structural or functional characteristics that would identify the modified chemokines that are disclosed as representative of the claimed genus. There is no guidance to allow one of skill in the art to identify other species with the same characteristics that are variants of or completely unrelated to these disclosed species. The claimed chemokines are not structurally related, the modifications are not structurally related, and the claims encompass all possible alterations to the known chemokine sequences. Appellant has not described the common attributes possessed by the members of the genus. The structural characteristics of four closely related sequences, and the functional characteristics of one species, do not provide compensatory guidance by which one of skill in the art could identify other members of the genus. No features are described that

these species have in common with structurally unrelated molecules by which one of skill would be able to identify them as members of the same genus. No structural or functional relationships or other essential characteristics are disclosed. While Appellant is in possession of amino-terminal modifications to SDF-1 molecules that exhibit enhanced function, the claims encompass not only structurally unrelated chemokines, but also all possible variants of these chemokines, as well as chemokines having one or more amino-terminal modification, which for claims 1, 5-14, 17, and 18 are selected from a group of structurally unrelated molecules. Thus, one of skill in the art would not conclude that Appellant had described the characteristics of the claimed genus by disclosing four closely related molecules. Thus, the claims contain subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Appellant, at the time the application was filed, had possession of the claimed invention

(b) Claims 1-14, 17, and 18 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for met-SDF-1beta, does not reasonably provide enablement for any other amino-terminally modified chemokines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection is set forth in prior Office Actions of Paper No. 8, Paper No. 12, Paper No. 14, and Paper No. 18 and summarized below.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte*

Forman, (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

As stated above, the claims include polynucleotides encoding modified chemokines that are unrelated in structure. They further include a potentially infinite number of variants of these modified chemokines, as well as chemokines with more than one amino-terminal modification, which for claims 1, 5-14, 17, and 18 may be selected from a group of structurally unrelated molecules. Appellant has disclosed the functional properties of one molecule, met-SDF-1 beta, which exhibits enhanced function relative to the unmodified chemokine. However, Appellant has not described the structural features or other characteristics of this molecule that would enable one of skill in the art to predictably identify and use polynucleotides encoding other amino-terminally modified chemokines, including polynucleotides comprising met-SDF-1 beta and structurally unrelated polynucleotides. The amino acid sequence of an encoded polypeptide determines its structural and functional properties, and predictability of what effects additions or variations within a sequence will have is complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure and function from mere sequence data are limited. While the generation of modified proteins is standard in the art, the disclosure of the functional properties of one species is not sufficient to allow one of skill to predict which, if any, of the potentially infinite number of molecules potentially within the scope of the claims could be used like met-SDF beta, or how else they might be used. MPEP §2154.03 states:

...if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is a lack of predictability in the art...in applications directed to inventions in the art where the results are unpredictable, the disclosure of

a single species usually does not provide an adequate basis to support generic claims. This is because it is not obvious from the disclosure of one species, what other species will work.

In the instant application, Appellant has disclosed the functional characteristics of only one species, and has not provided any guidance by which other functional species might be identified. Appellant's disclosure thus does not bear a reasonable correlation to the scope of the claims, which as stated above, encompass a widely divergent species, including molecules structurally unrelated to what is disclosed and enabled. Absent further guidance, one of skill in the art would be able to make the claimed molecules, but would not be able to predict which ones would function. Because one of skill would not be able to predict which of the many possible embodiments of the claims could actually be used, it would require undue experimentation to practice the invention as broadly claimed. Appellant has thus not provided sufficient information for the skilled artisan to use the invention commensurate with the scope of the claims.

(11) Response to Argument

Appellant has argued the written description and scope of enablement rejections alternately on pages 4-13 of the Appeal Brief. Appellant's arguments with respect to the written description rejection are addressed together, immediately below. Appellant's arguments with respect to the scope of enablement rejection are addressed together, subsequent to the response to Appellant's arguments with respect to the written description rejection.

(a) Appellant argues on p. 4 that claims 1-14, 17, and 18 are drawn to a specifically enumerated set of amino-terminal modified chemokines. Appellant further argues on p. 5 that these chemokines are sufficiently described in the specification to convey to one of ordinary skill

in the art that Appellants were in possession of the claimed invention. Appellant states on p. 5 that the specification must convey with reasonable clarity that Appellant was in possession of the invention, citing *In re Gostelli* and *Vas-Cath, Inc. v. Maharkar*. Appellant additionally states on p. 5 that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed and cites *In re Wertheim* and *In re Marzocchi*. On pages 8 and 9, Appellant argues that the Examiner has impermissibly read a functional limitation into the claims. Appellant also argues on p. 8 that the claims read on compositions comprising chemokines from an enumerated list with amino-terminal modifications and that the invention as claimed does not require knowledge of the structural and functional characteristics of the amino-terminal modified chemokines. Appellant states that the Examiner has stated that the claims must be viewed as reading on the functional characteristics of the modified chemokines. Appellant argues on p. 9 that Appellant has more than met the requirement for reasonable clarity. Appellant points to Example 1 as detailing methods used to construct amino-terminal modified chemokines and further states that the chemokines of claims 1-5, 10-14, 17, and 18 belong to the C-C, CXC, or CX3C class of chemokines and were well known in the art before the filing date of the application. Appellant argues on p. 10 that one of ordinary skill in the art would recognize that Appellant was in possession of the invention as claimed and concludes that the Examiner has not met her burden of presenting by a preponderance of the evidence why a person in the art would not recognize in Appellant's disclosure a description of the invention as defined by the claims.

Appellant argues on p. 10 that the above arguments apply to claims 6-9 and that these claims are separately patentable because they read on a narrower subset of modified chemokines than claims 1-5, 10-14, 17, and 18.

Appellant's arguments have been fully considered but have not been found to be persuasive. As stated above and in the rejections of paper nos. 8 and 12 as well as the advisory actions of paper nos. 14 and 18, the claims encompass not only specific enumerated molecules, but also variants and sequences comprising them. As stated above, Appellant has defined a modified chemokine derived from a chemokine as including "any kind of alteration, addition, insertion, deletion, mutation, substitution, replacement, or other modification (p. 17 of the specification). Claims 6-9 limit only to sequences comprising "amino-terminal" fragments and sequences identified by hybridization. Claims 17 and 18 have only a functional limitation, that the molecule bind to a particular receptor. Thus, rather than being limited to a finite number of additions to a finite number of molecules, the claims encompass a potentially infinite number of variants and sequences comprising them, as well as molecules defined only by their binding ability. They are thus drawn to a genus of molecules, rather than a set of particularly defined entities. Thus, in order for one of skill in the art to recognize that Appellant was in possession of the genus, some common characteristic must be set forth. That the molecules belong to one of three classes of chemokines does not serve to identify them; there are no common features that are supplied by this identification. The USPTO written description guidelines (Federal Register, Vol. 66, No. 4, January 6, 2001, p. 1106) indicate, for each claim drawn to a genus:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice...reduction to drawings...or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed

correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus...

Appellant has disclosed four closely related species, amino-terminally modified forms of SDF-1 alpha and beta. The molecules claimed include a structurally unrelated group of factors and variants thereof. Thus, they need have no structure in common with eachother or with the four disclosed species. The Examiner did not state that the claims must be viewed as reading on the functional characteristics of the modified chemokines; what was stated in the advisory action of paper no. 14 was that the functional characteristics were essential to what Appellant has described as the invention. The USPTO guidelines require on p. 1106 that the Examiner,

If the application as filed does not disclose the complete structure...of the claimed invention as a whole, determine whether the specification discloses other relevant identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Since Appellant states on p. 1 of the specification that the invention relates to the use of the amino-terminally modified chemokines to inhibit the interaction between chemokine receptors and their naturally occurring ligands, this property was considered as a "relevant identifying characteristic". However, Appellant has argued that they need have no common function. Since, then, Appellant has set forth no common function, the molecules have no common structure or other physical or chemical properties, and has further not taught what there is about the four closely related molecules that Appellant has generated that is representative of the genus, Appellant has not described the claimed genus of sequences comprising amino-terminally modified chemokines, as defined by Appellant on p. 17 of the specification, with reasonable

clarity. One of skill in the art would therefore not conclude that Appellant was in possession of the claimed genus at the time of filing.

Appellant argues that claims 6-9 are more narrowly drawn. However, these claims encompass sequences comprising only fragments, as well as molecules identified only by hybridization. They therefore also encompass large numbers of molecules that need have no sequences in common, and thus, for the reasons set forth above, the skilled artisan would not conclude that Appellant was in possession of the claimed genus.

(b) Appellant argues on p. 5 that the specification provides more than enough detail to enable the invention as claimed. Appellant, quoting from MPEP §2164, states on p. 6 that the standard for determining enablement requires that any person skilled in the art be able to make and use the invention without undue experimentation. Appellant states that a patent need not teach and preferable omits what is known in the art. Appellant states that complex experimentation is not necessarily undue. Appellant refers to the Wands factors on p. 7, which are set forth above, and notes that it is improper to conclude that the disclosure is not enabling based on analysis of only one factor. Appellant states that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, the enablement requirement is satisfied (pages 7 and 8). On p. 11, Appellant states that the Examiner concedes that one of skill would be able to make the modified chemokines, but "expresses reservations as to whether the disclosure enables the use of the invention". Appellant argues on p. 11 that the characterization of Appellant's invention as inhibitors of receptor/ligand binding is incomplete and that the invention can be used for identifying cells expressing receptors, as vaccine adjuvants, to enhance the activity of

antigen-presenting cells, to affect the chemotactic recruitment of migratory cells, and to "affect the nature of chemokine-receptor interactions". Appellant argues that examples 2-6 provide protocols for various uses. Appellant states that "if there is considerable direction and guidance in the specification, if there is a high level of skill in the art at the time the application was filed, and if all of the methods needed to practice the invention are either disclosed in the specification or well known, then the specification is enabling with respect to the claims at issue. Appellant further argues on p. 12 that working examples are disclosed. Appellant argues that the Examiner's statement that one of ordinary skill would not be able to predict which molecules would function in accordance with the invention incorrectly states the enablement requirement. Appellant reiterates that the test is whether one of skill could make and use the invention without undue experimentation. Appellant argues that the enablement requirement does not require that the disclosure "provide any type of prediction with respect to the end results". Appellant further argues that a "detailed road map has been provided" and submits that the "use" aspect of the claimed invention has also been met.

Appellant's arguments have been fully considered but have not been found to be persuasive. The Examiner agrees that one of ordinary skill could make any particular modified cytokine. However, the claims were rejected because the skilled artisan could not use the invention as broadly claimed. As stated above, the claims encompass a potentially infinite number of molecules. Furthermore, even the effect of the claimed amino-terminal modifications on known molecules is unpredictable: as stated in the office action of paper no. 8, one of the claimed modifications had precisely the opposite effect on another chemokine, RANTES, than it did on Appellant's single disclosed working example, SDF-1 beta (Proudfoot et al., J. Biol.

Chem., 1996, vol. 271, pages 2599-2603). Thus, the claims encompass many possible embodiments, and the effect of the claimed modification, as well as the effects of the variations encompassed by the claims, is unpredictable. Appellant argues that the invention has uses other than inhibition of receptor/ligand interactions and points to examples 2-6. However, what these examples show are various effects of met-SDF-1 beta. Thus the working examples demonstrate only the uses of one modified molecule. There is nothing presented to indicate that any other molecules, including those that are structurally unrelated to met-SDF-1 beta, would have similar effects. There is nothing in the specification to show or to allow one of skill to predict what effects such molecules might have and thus to what uses they could be put. Appellant argues that predictability is not required. However, predictability is one of the Wands factors cited by Appellant (p. 7). Further, MPEP §2164 states

> ... in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity).

Predictability is thus a factor to be considered when considering issues of enablement.

MPEP §2164 further states:

> The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability.

...The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. ' " In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

The art teaches, as indeed Appellant shows, that small changes can affect the functional characteristics of known molecules. The effects of such changes are unpredictable, as recognized by the courts and as evidenced by the teachings of Proudfoot et al., cited above. The claims encompass many structurally unrelated embodiments, and what Appellant has provided are the functional characteristics of one such embodiment. This is not a "detailed road map": there is no guidance as to which of the many possible embodiments of the claimed invention could actually be used, either as inhibitors or in the other ways Appellant suggests. The specification thus does not "provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed".

Thus, the claims are broadly drawn: they encompass not only known chemokines, on which the effects of the claimed modification has not been shown and could not readily be predicted, but also any variants of these chemokines as well as sequences comprising the modified chemokines and such variants. The nature of the invention is similarly broad: Appellant sets forth many possible uses for all of these molecules. The prior art teaches that the effects of changes to biochemical molecules in general are unpredictable. The guidance and working examples provided are limited to the use of only one molecule, met SDF-1 beta. Thus, the claims encompass many different and unrelated molecules, there is no guidance as to which could be used as taught by Appellant, and there are no teachings to allow one of skill to predict which could be used. The skilled artisan would therefore have to test each potential embodiment

for any or all of the activities suggested by Appellant, with no ability to predict whether such testing would be successful. It would therefore require undue experimentation to use Appellant's invention as broadly claimed.

Appellant argues that claims 6-9 are separately patentable because they read on a narrower subset of modified chemokines. However, these claims encompass sequences comprising fragments as well as sequences identified by homology. They thus encompass sequences that vary widely from what is disclosed, and the skilled artisan would not predictably be able to use such molecules as disclosed by Appellant.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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